Amitriptyline HCl Tablets, USP
10mg, 25mg, 50mg, 75mg, 100mg and 150mg
ANDA # 40-218
Reviewer: A.P.Patel
File:x:\wpfile\biofinal\ 40218sdw.n96

Vintage
Charlotte, NC
Submission Date:
Nov. 1, 1996

REVIEW OF BIO-STUDY, DISSOLUTIONS AND 5 WAIVER REQUESTS

INTRODUCTION:

Amitriptyline hydrochloride is a tricyclic antidepressant indicated for the relief of symptoms of depression. It is presumed to act by interference with the transport, storage and release of catecholamines.

BACKGROUND:

Amitriptyline hydrochloride is an "AB" rated drug and 25 mg Elavil^{R} tablet is the reference listed drug manufactured by Zeneca. The drug is available in tablets 10, 25, 50, 75, 100 and 150 mg strengths and 10 mg/ml injection.

Objective:

The purpose of this study was to compare the relative bioavailability of Vintage's 25 mg amitriptyline HCl tablets with that of 25 mg Elavil^{R} tablets taken under fasting conditions in healthy, adult, male subjects.

Summary of Bioequivalence Study Procedures:

A. **BE Study under Fasting Conditions:**
25 mg bio-study

1. Protocol No. VIN-501 and Study# 9528043D

2. **Objective of the study:**
The objective of this study is to determine the bioequivalence of amitriptyline hydrochloride formulation after administration of single doses to healthy volunteers under fasting conditions.

3. **Study Design:**
A randomized, single-dose, two-period, two-treatment, two-sequence crossover study was conducted assessing the relative bioavailability of Vintage's Amitriptyline hydrochloride 2x25 mg tablets vs. Zeneca's Elavil® 2x25 mg tablets under fasting condition.

4. **INVESTIGATOR AND FACILITIES**

A. **INVESTIGATOR**

(b)4 - Confidential Business

B. **STUDY SITE**

(b)4 - Confidential Business

C. **LABORATORIES**

Samples for clinical safety analysis (urine drug screening, chemistry,

(b)4 - Confidential Business

D.

(b)4 - Confidential Business

5. **Study dates:** Period 1 12/02/95
Period 2 12/16/95

6. **Drug Products:**
25 mg Tablets:
A. Test: 2x25 mg Amitriptyline hydrochloride Tablets (Vintage, Lot #031104A, batch size (b)4 Exp. Date 10/96)
B. Reference: 2x25 mg Elavil® Tablets (Zeneca, Lot #3120P, Exp. 10/96).

All doses were administered with 240 ml water following an overnight fast.

7. **Subjects:** Thirty-two (32) healthy male volunteer subjects were recruited for this study (30 completed) between ages of 18 - 49, with a mean (± s.d.) age of 31.8 ± 8.3 years, and within 15% of their ideal weight as specified in the protocol. All subjects were selected based on the medical history, physical examination and clinical laboratory evaluations showing absence of any clinically significant findings. Inclusion and exclusion criteria in the protocol were followed in the selection of the subjects.

8. **Confinement:** At least 8 hours pre-dose to at least 24 hours post-dose administration, each period. The subjects were housed and fed at the clinical facility.

9. **Food and fluid intake:** Standardized meals and beverages. No caffeine or

xanthine-containing food or drink was allowed during confinement. The drug products were administered with 240 ml of water following 8 hour fast. Water was allowed ad lib. after 2 hours post-dose.

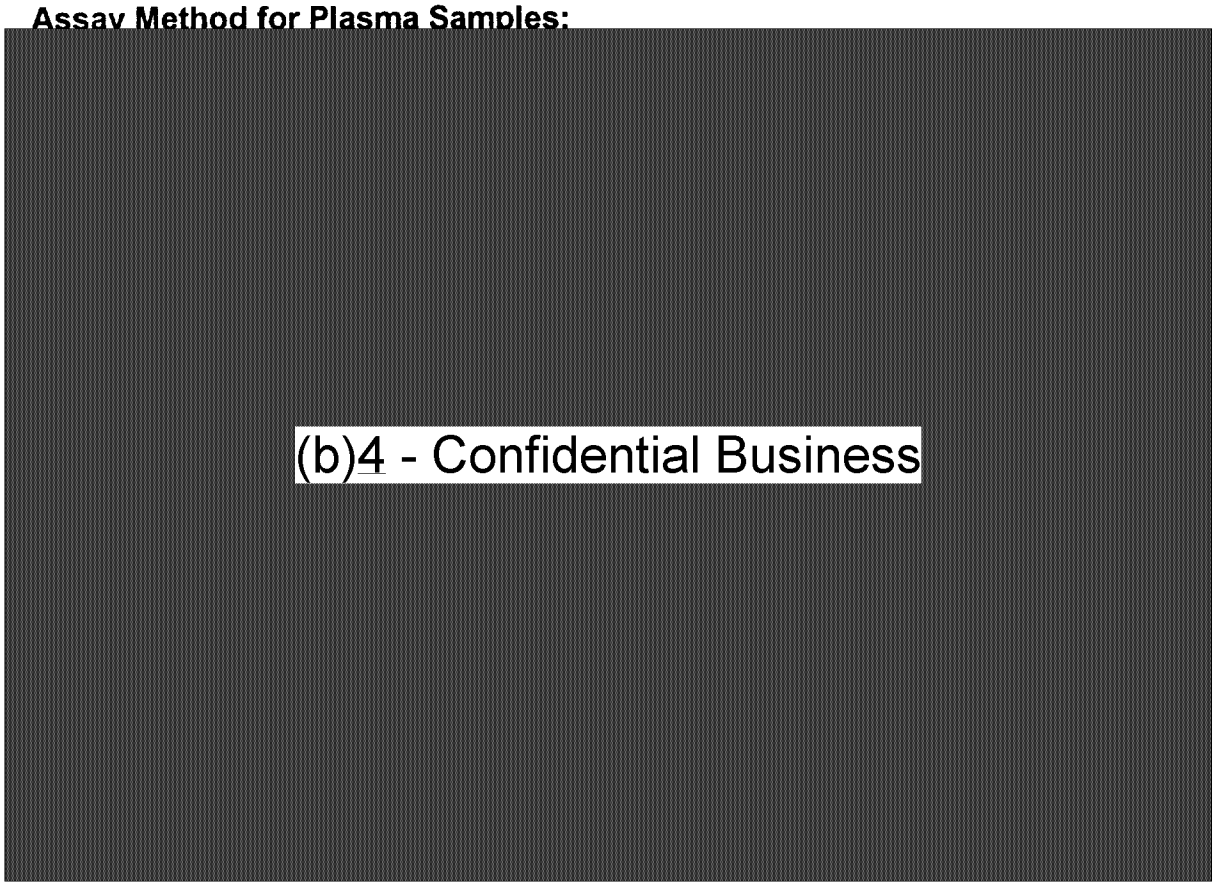
10. **Washout period:** 2 weeks

11. **Blood samples:** In each period, 10 ml of blood samples were collected in EDTA containing purple-top tubes at 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 15, 24, 36, 48, 72, 96, 120, 144, and 168 hours. Plasma was separated and were stored frozen at -20°C or below until analyzed.

12. **Subject safety monitoring:** Subjects were asked to spontaneously report any signs or symptoms that might be related to the drug products.

13. **Adverse events:** Following each dosing period subjects were asked to report any signs or symptoms judged to be drug related.

14. **Assay Method for Plasma Samples:**



15. **Pharmacokinetics and statistical analysis:** Statistical analyses were performed on the pharmacokinetics parameters for plasma amitriptyline and nortriptyline. The 90% confidence intervals were calculated for AUCt, AUCi and Cmax.

D. In Vivo Results:

Thirty-two (32) healthy male volunteer subjects were recruited for this study and 30 completed the study. Subject 11 did not return for the period 1 return blood samples and was withdrawn from the study. He received one dose of the test treatment. Subject 31 was withdrawn from the study on day 1 of period 1 because he refused to follow study procedures. He received one dose of the reference treatment. The data from subject 27 were not reported because the subject's samples contained numerous interfering chromatographic peaks that prevented measurement of both analyte. All the available data from 29 subjects with reported amitriptyline and nortriptyline concentrations were used in the pharmacokinetic analyses. There were 39 adverse events reported of which 54% were with test and 46% were with reference drug. None of the events were of clinical significance.

Table 1. Summary of amitriptyline Plasma concentration and PK parameters.

AMITRIPTYLINE (ng/ml)					
Time	Test		Reference		Ratio
(h)	Mean	CV%	Mean	CV%	T/R
0.0	0.00	.	0.00	.	0.00
1.0	3.02	91.98	2.96	97.00	1.02
2.0	16.11	55.30	14.33	54.03	1.12
3.0	20.88	40.78	20.62	49.94	1.01
4.0	22.32	33.14	20.76	40.16	1.08
5.0	21.85	30.44	21.13	37.18	1.03
6.0	20.04	31.41	20.27	40.85	0.99
7.0	19.06	32.36	18.42	42.11	1.03
8.0	17.69	39.56	16.37	42.28	1.08
9.0	15.53	34.38	14.71	44.04	1.06
10.0	13.82	33.24	13.38	52.80	1.03
12.0	10.96	36.27	10.42	45.41	1.05
15.0	8.93	38.98	8.77	50.15	1.02
24.0	6.57	43.91	5.92	44.71	1.11
36.0	3.97	52.77	3.64	52.27	1.09
48.0	2.91	50.30	2.66	54.18	1.09
72.0	1.39	75.93	1.20	76.95	1.16
96.0	0.66	101.62	0.58	104.33	1.15
120.0	0.24	185.78	0.22	191.80	1.11
144.0	0.14	212.49	0.09	225.90	1.56
168.0	0.03	529.15	0.03	373.93	0.83
AUCT (ng.h/ml)	473.16	44.08	443.39	48.67	1.07
AUCINF (ng.h/ml)	511.56	41.11	469.84	45.73	1.09
CMAX (ng/ml)	24.79	32.66	23.27	41.05	1.07
TMAX (h)	4.48	36.07	4.59	26.41	0.98
KEL (h-1)	0.03	32.35	0.03	30.81	0.98
Halflife (h)	24.87	30.21	24.03	28.02	1.03

	Means			Ratio	90% CI	log-transf
	Test		Reference	T/R	lower	upper
LAUCT (ng.h/ml)	6.07		6.00	1.01	1.01	1.15
LAUCINF (ng.h/ml)	6.16		6.07	1.02	1.01	1.15
LCMAX (ng/ml)	3.16		3.07	1.03	1.00	1.18

(PK Parameters and 90% confidence limits were verified)

Amitriptyline HCl: AUCt:AUCinf, ratios for Test and Reference product

TRTMNT= Test

SUBJECT	AUCT	AUCINF	RAUC
1	445.85	459.68	0.96992
2	166.60	177.42	0.93902
3	635.10	668.85	0.94954
4	678.35	703.21	0.96465
5	284.10	314.59	0.90308
6	387.00	406.15	0.95285
7	464.45	483.63	0.96033
8	388.70	406.01	0.95736
9	206.80	233.74	0.88473
10	307.55	332.43	0.92516
12	703.26	725.02	0.96999
13	365.80	415.70	0.87997
14	634.75	651.15	0.97482
15	398.51	413.93	0.96276
16	1210.02	1251.53	0.96684
17	590.99	632.28	0.93469
18	643.20	695.27	0.92511
19	436.80	464.21	0.94095
20	645.75	675.38	0.95613
21	423.15	437.14	0.96799
22	541.00	589.12	0.91832
23	312.36	358.80	0.87059
24	471.40	497.60	0.94734
25	534.10	588.96	0.90685
26	282.20	297.03	0.95007
28	632.10	661.10	0.95613
29	323.30	376.66	0.85833
30	216.57	247.58	0.8747
32	391.82	407.17	0.96230

TRTMNT= Reference

SUBJECT	AUCT	AUCINF	RAUC
1	315.102	335.506	0.93918
2	213.447	235.429	0.90663
3	515.450	542.037	0.95095
4	862.550	884.782	0.97487
5	320.200	361.682	0.88531
6	412.150	431.131	0.95597
7	366.550	385.827	0.95004
8	323.450	335.788	0.96326
9	142.500	157.945	0.90221
10	290.550	315.728	0.92025
12	614.432	637.014	0.96455
13	365.700	405.821	0.90114
14	482.613	498.684	0.96777
15	474.250	511.743	0.92674
16	1225.80	1247.21	0.98284
17	567.50	603.51	0.94034
18	607.20	627.83	0.96714
19	321.40	345.76	0.92955
20	618.38	641.32	0.96422
21	431.25	448.22	0.96214
22	468.60	498.51	0.94001
23	269.70	315.75	0.85416
24	265.60	296.18	0.89674
25	480.30	514.10	0.93426
26	386.35	402.08	0.96089
28	617.34	642.35	0.96106
29	313.52	358.99	0.87332
30	238.2	255.84	0.93107
32	348.26	388.64	0.89610

Figure 1. Mean Plasma Amitriptyline

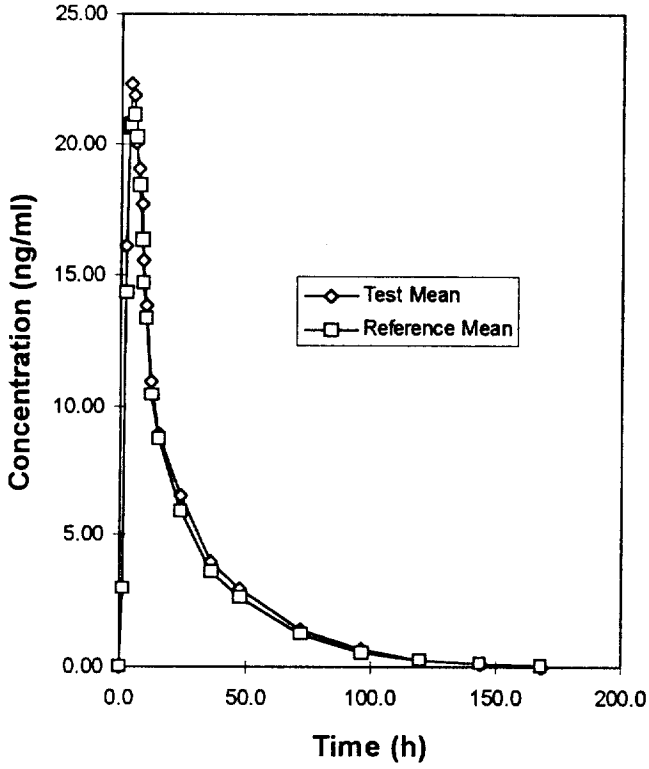
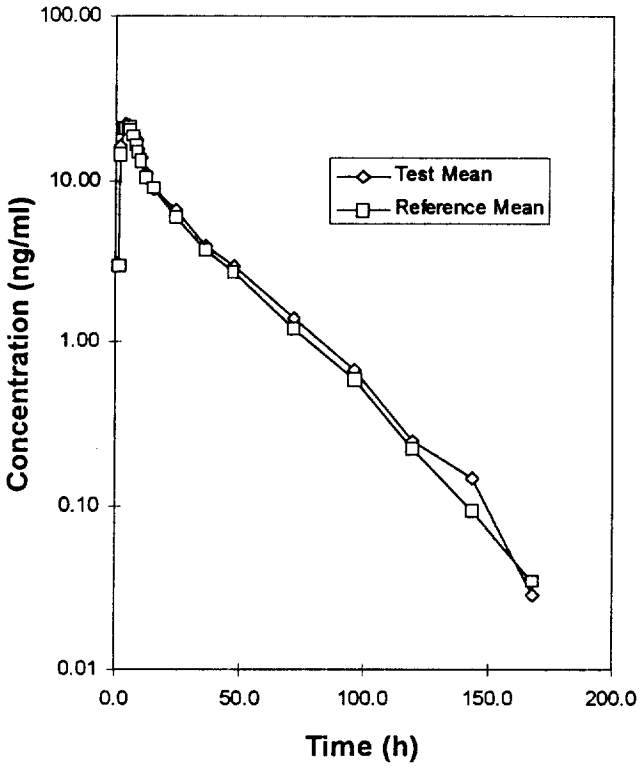


Figure 2. Mean Plasma Amitriptyline (semilog plot)



The amitriptyline mean lnAUCt, lnAUCinf and lnCmax 90% C.I. are within the acceptable range of 80-125% (Table 1). The nortriptyline mean lnAUCt, lnAUCinf and lnCmax 90% C.I. are within the acceptable range of 80-125% (Table 2). The bio-study under fasting condition is acceptable.

Table 2. Summary of nortriptyline Plasma concentration and PK parameters.

		NORTRIPTYLINE (ng/ml)					
Time	Test		Reference		Ratio		
(h)	Mean	CV%	Mean	CV%	T/R		
0.0	0.00	.	0.00	.	0.00		
1.0	0.18	193.82	0.24	156.79	0.73		
2.0	1.88	66.01	1.88	67.18	1.00		
3.0	3.32	44.39	3.24	65.63	1.03		
4.0	3.94	41.14	3.68	49.10	1.07		
5.0	4.70	51.75	4.40	44.24	1.07		
6.0	5.46	40.62	5.43	45.08	1.00		
7.0	5.94	39.22	5.84	40.59	1.02		
8.0	6.18	37.34	6.07	42.26	1.02		
9.0	6.27	38.88	6.01	42.05	1.04		
10.0	6.16	38.58	5.90	39.96	1.05		
12.0	6.24	43.48	5.97	40.52	1.04		
15.0	6.02	40.57	5.76	41.10	1.05		
24.0	5.50	39.59	5.24	39.47	1.05		
36.0	5.06	45.23	4.63	45.41	1.09		
48.0	4.32	54.58	3.88	52.15	1.11		
72.0	3.12	61.98	2.84	58.04	1.10		
96.0	2.04	70.99	1.82	68.28	1.12		
120.0	1.48	82.64	1.37	81.02	1.08		
144.0	0.95	103.85	0.79	101.84	1.21		
168.0	0.63	123.83	0.50	134.80	1.26		
AUCT (ng.h/ml)	480.91	54.08	440.43	51.91	1.09		
AUCINF (ng.h/ml)	545.91	56.31	501.56	52.41	1.09		
CMAX (ng/ml)	6.96	38.80	6.59	41.00	1.05		
TMAX (h)	12.00	53.54	12.93	83.19	0.93		
KEL (h-1)	0.02	40.11	0.02	33.96	1.08		
Halflife (h)	40.73		42.75		0.95		
	Geometric Means				Ratio	90% CI	log-transf
	Test		Reference		T/R	lower	upper
LAUCT (ng.h/ml)	404.63		374.84		1.08	1.03	1.14
LAUCINF (ng.h/ml	459.12		431.41		1.06	1.01	1.12
LCMAX (ng/ml)	6.46		6.05		1.07	1.02	1.12

(PK Parameters and 90% confidence intervals were verified)

Nortriptyline HCl: AUCt:AUCinf, ratio for Test and Reference Product

TRTMNT= TEST

SUBJECT	AUCT	AUCINF	RAUC
1	60.500	99.05	0.61083
2	431.400	459.06	0.93975
3	873.550	1072.63	0.81440
4	731.500	812.51	0.90030
5	203.650	226.65	0.89853
6	358.850	384.16	0.93411
7	882.375	1061.30	0.83141
8	350.800	423.95	0.82745
9	312.500	330.48	0.94560
10	807.900	994.76	0.81216
12	300.070	332.26	0.90312
13	144.950	157.87	0.91815
14	891.700	991.65	0.89921
15	308.440	334.97	0.92080
16	337.688	371.92	0.90795
17	757.182	887.13	0.85352
18	969.750	1118.94	0.86667
19	175.850	196.48	0.89498
20	470.400	557.40	0.84392
21	578.650	600.52	0.96359
22	661.850	751.21	0.88105
23	510.349	532.79	0.95788
24	327.900	362.54	0.90446
25	771.700	851.75	0.90601
26	306.850	368.86	0.83190
28	549.150	609.77	0.90058
29	171.250	184.03	0.93058
30	309.032	346.23	0.89256
32	390.496	410.60	0.95103

TRTMNT=REFERENCE

SUBJECT	AUCT	AUCINF	RAUC
1	48.050	83.382	0.57626
2	407.137	432.032	0.94238
3	720.700	853.596	0.84431
4	666.150	742.757	0.89686
5	206.300	241.891	0.85286
6	335.400	389.668	0.86073
7	772.250	904.339	0.85394
8	318.400	354.339	0.89857
9	241.450	273.018	0.88437
10	818.100	934.354	0.87558
12	289.117	340.179	0.84990
13	142.800	161.504	0.88419
14	723.014	845.413	0.85522
15	303.400	339.00	0.89499
16	295.300	325.12	0.90828
17	783.450	870.98	0.89950
18	926.950	1066.98	0.86876
19	144.050	175.48	0.82088
20	428.663	537.35	0.79774
21	543.800	612.56	0.88774
22	540.700	567.46	0.95284
23	321.800	344.82	0.93324
24	344.400	382.41	0.90060
25	511.350	564.47	0.90590
26	385.300	442.78	0.87018
28	591.840	708.19	0.83571
29	222.558	253.11	0.87930
30	363.800	398.23	0.91354
32	376.103	399.90	0.94049

Figure 3. Mean Plasma Nortriptyline

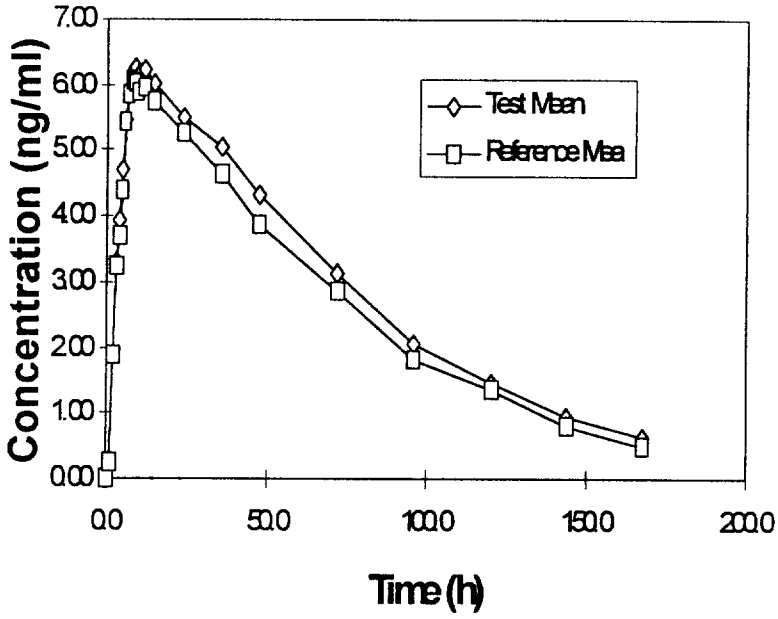
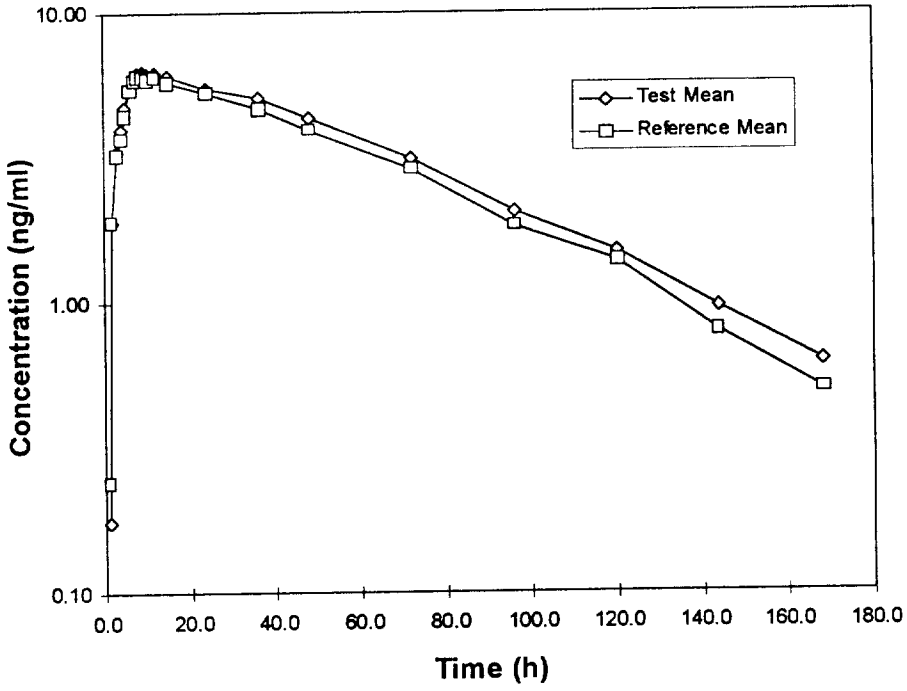


Figure 4. Mean Plasma Nortriptyline (semilog plot)



E. Components and Composition:

Vintage's formulations for 10 mg, 25mg, 50mg, 75mg, 100mg, and 150mg tablets are shown as attachments.

F. Dissolution:

The method and results are presented in Table 3, and are acceptable.

Table 3. In Vitro Dissolution Testing

Generic Drug: Amitriptyline HCl
Dose Strength: 10 mg, 25 mg, 50 mg, 75 mg, 100 mg and 150 mg Tablets
ANDA #: 40-218
Firm: Vintage Pharmaceuticals, Inc.

I. Dissolution Testing Method: **USP 23 Method, pp93-94.**

USP XXIII Apparatus: 1 (basket) RPM: 100
No. Units Tested: 12
Medium: 0.1 N Hydrochloric acid Volume: 900 ml Temperature: 37°C
Tolerance: NLT (b)4 of Amitriptyline HCl (Q) in 45 minutes
Reference Drug: Elavil made by Zeneca
Assay Methodology: Validated method

II. Results of In Vitro Dissolution Testing:

Sampling Times (Minutes)	Test Product LOT# 030104 Strength 10 mg			Reference Product LOT # 3487P Strength 10 mg		
	Mean %	Range	S.D.	Mean %	Range	S.D.
10	95.6	(b)4 - Confidential Business	3.7	48.8	(b)4 - Confidential Business	11.7
21	98.4		2.8	89.2		7.4
33	100.1		3.3	101.0		4.5
45	**100.3**		**2.7**	**101.2**		**2.9**

Sampling Times (Minutes)	Test Product LOT # 031104 Strength 25 mg			Reference Product LOT # 3787P Strength 25 mg		
	Mean %	Range	S.D.	Mean %	Range	S.D.
10	80.4	(b)4 - Confidential Business	6.9	67.3	(b)4 - Confidential Business	5.6
21	100.3		1.8	97.8		2.2
33	101.3		1.8	99.8		2.2
45	**101.2**		**1.8**	**99.8**		**2.1**

Sampling Times (Minutes)	Test Product LOT # 037104 Strength 50 mg			Reference Product LOT #3593P Strength 50mg		
	Mean %	Range	S.D.	Mean %	Range	S.D.
10	63.1	(b)4 - Confidential Business	10.3	61.4	(b)4 - Confidential Business	5.3
21	100.9		3.5	98.6		2.9
33	102.6		3.6	101.8		2.2
45	**102.4**		**4.1**	**102.6**		**1.1**

Sampling Times (Minutes)	Test Product LOT# 032104 Strength 75 mg			Reference Product LOT # 5327N Strength 75 mg		
	Mean %	Range	S.D.	Mean %	Range	S.D.
10	70.2	(b)4 -	4.7	52.3	(b)4 -	5.0
21	100.1		2.3	93.7		4.2
33	101.3	Confidentia	2.3	101.5	onfidentia	2.9
45	**102.6**	Business	**2.2**	**100.7**	Business	**2.5**

Sampling Times (Minutes)	Test Product LOT# 033104 Strength 100 mg			Reference Product LOT # 3725P Strength 100 mg		
	Mean %	Range	S.D.	Mean %	Range	S.D.
10	48.0	(b)4 -	4.4	38.8	(b)4 -	2.8
21	91.9		4.4	80.4		5.2
33	98.4	onfidentia	2.8	99.6	onfidentia	2.4
45	**100.0**	Business	**2.8**	**101.4**	Business	**3.1**

Sampling Times (Minutes)	Test Product LOT# 034104 Strength 150 mg			Reference Product LOT # 5306N Strength 150 mg		
	Mean %	Range	S.D.	Mean %	Range	S.D.
10	54.8	(b)4 -	13.1	37.4	(b)4 -	4.4
21	97.2		6.6	76.8		4.1
33	101.2	onfidentia	4.4	96.0	onfidenti	4.0
45	**99.9**	Business	**3.7**	**97.7**	Business	**4.4**

E. Comments:

1. The firm's in vivo bioequivalence study under fasting conditions is acceptable. The test product is similar in both rate and extent of absorption to the reference product. The 90% confidence intervals for lnAUCt, lnAUCinf and lnCmax are within the acceptable range of 80 - 125% for amitriptyline and nortriptyline. Nortriptylene plasma concentration for subject #1 were not detectable after 36 hour time point. Amitriptyline AUCinf and Kel for subject #30 were not determined.

2. The in vitro dissolution testing submitted by the firm on its Amitriptyline HCl 10, 25, 50, 75, 100 and 150 mg tablets is acceptable.

3. The formulations for Amitriptyline HCl 10, 50, 75 100, and 150 mg tablets are proportionally similar to the 25 mg strength of the test product used for bioequivalence study.

4. FOR INTERNAL USE ONLY: *It is OGD's normal practice for this dru*

(b)5 - Gov't Pre-Decisional

F. Deficiency: None

Recommendations:

1. The bioequivalence study conducted by Vintage, Inc., under fasting conditions on its Amitriptyline HCl, 25 mg Tablet, LOT # 031104, comparing it to Zeneca's Elavil[R] 25 mg Tablet has been found acceptable by the Division of Bioequivalence. The study demonstrated that Vintage's Amitriptyline HCl Tablet, 25 mg is Bioequivalent to the reference product, Elavil[R], 25 mg Tablet, manufactured by Zeneca.

2. The dissolution testing conducted by the firm on its Amitriptyline HCl Tablets, 10 mg (LOT# 030104), 25 mg (LOT # 031104), 50 mg (LOT # 037104),75 mg (LOT# 032104), 100 mg (LOT# 033104) and 150 mg (LOT# 034104) is acceptable. The 10 mg, 50 mg, 75 mg, 100 mg and 150 mg formulations are proportionally similar to the 25 mg strength of the test product which underwent acceptable bioequivalence testing. Waivers of in vivo bioequivalence study requirements for the 10 mg, 50 mg, 75 mg, 100 mg and 150 mg strength tablets of the test product are granted. The Division of Bioequivalence deems Amitriptyline HCl Tablets 10 mg, 50 mg, 75 mg, 100 mg and 150 mg, manufactured by Vintage, Inc., to be Bioequivalent to Elavil[R] 10 mg, 50 mg, 75 mg, 100 mg and 150 mg Tablets, manufactured by Zeneca.

3. The dissolution testing should be incorporated into the firm's manufacturing controls and stability program. The dissolution testing should be conducted in 900 ml of 0.1 N HCl at 37°C using, USP 23 apparatus I (basket) at 100 rpm. The test product should meet the following specifications:

   Not less than (b)(4)Q) of the labeled amount of the amitriptyline.HCl in the dosage form is dissolved in 45 minutes.

The firm should be informed of the above recommendations.

/S/ 4/23/97

A.P.Patel
Division of Bioequivalence
Review Branch III

RD INITIALED RMHATRE
FT INITIALED RMHATRE
/S/ Date: 4/24/97
Ramakant M. Mhatre, Ph.D.
Chief, Branch III
Division of Bioequivalence

Concur
/S/ Date: 4/30/97
Nicholas M. Fleischer, Ph.D.
Director
Division of Bioequivalence

cc: ANDA# 40-218 (Original, Duplicate), A.P.Patel, Drug File, Division File.

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: November 25, 1996

FROM: Anna Marie H. Weikel
Consumer Safety Officer
Regulatory Support Branch, HFD-615

SUBJECT: ANDA 40-218

TO: Rabi Patnaik, Ph.D.
Acting Director of Division of Bioequivalence

THROUGH: Mark Anderson
Project Manager
Division of Bioequivalence

ntage Pharmaceuticals, Inc. has submitted an application containing six strengths of Amitriptyline. Included in the application is a bioequivalence study for the 25 mg strength and a request for a waiver of in vivo bioequivalence for the 10 mg, 50 mg, 74 mg, 100 mg, and 150 mg strengths. This is a deviation from OGD policy which does not normally permit more than three strengths to be waived by a single bioequivalence study.

Please comment on whether the submitted bioequivalence study would permit waivers to be granted for the other five strengths.

Thank you in advance.

Amitriptyline Hydrochloride
Tablets

Six strengths (10, 25, 50, 75, 100, 150 mg) have been approved for this drug product. The reference listed drug (RLD) is Zeneca's Elavil. The 25 mg srength of this drug product has been identified as the reference drug for conducting in vivo bioequivalence study. This lower strength was possibly chosen due to safety reasons. The Organge Book lists thirteen approved generic drug products for this drug. These products have been approved between 1983 and 1987. At this time, there seems to be no reason to change this strength as the reference drug strength. Concurrence of this continuing practice of DBE has been obtained from OGD (Doug Sporn) during the weekly Bio-Director's Meeting.

/S/ 2/28/97

Rabi Patnaik, Ph.D.
Division of Bioequivalence

VINTAGE PHARMACEUTICALS, INC.
Amitriptyline HCl Tablets, USP
10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg

COMPONENTS AND COMPOSITION STATEMENT
Amitriptyline HCl Tablets
10 mg

Ingredient	per tablet	Quantity per batch
Amitriptyline HCl, USP	10.00 mg	(b)4 -
Microcrystalline Cellulose, NF PH101	(b)4 - Confidential Business	
Lactose Monohydrate, NF DC		
Colloidal Silicon Dioxide, NF		
Sodium Starch Glycolate, NF		
Magnesium Stearate, NF		
Total	125.00 mg	(b)4 - Confidential

(b)4 - Confidential Business

10/28/96
Approved - Manufacturing Date

10/28/96
Approved - Regulatory Affairs Date

VINTAGE PHARMACEUTICALS, INC.
Amitriptyline HCl Tablets, USP
10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg

COMPONENTS AND COMPOSITION STATEMENT
Amitriptyline HCl Tablets
25 mg

Ingredient	per tablet	Quantity per batch
Amitriptyline HCl, USP	25.00 mg	[redacted]
Microcrystalline Cellulose, NF PH101	[redacted]	
Lactose Monohydrate, NF DC		
Colloidal Silicon Dioxide, NF		
Sodium Starch Glycolate, NF		
Magnesium Stearate, NF		
Total	125.00 mg	

(b)4 - Confidential Business

(b)4 - Confidential Business

(b)4 - Confidential Business

10/25/96
Approved - Manufacturing Date

12/25/96
Approved - Regulatory Affairs Date

VINTAGE PHARMACEUTICALS, INC.
Amitriptyline HCl Tablets, USP
10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg

COMPONENTS AND COMPOSITION
STATEMENT
Amitriptyline HCl Tablets
50 mg

Ingredient	per tablet	Quantity per batch
Amitriptyline HCl, USP	50.00 mg	
Microcrystalline Cellulose, NF PH101		
Lactose Monohydrate, NF DC	(b)4 -	
Colloidal Silicon Dioxide, NF	onfidenti	
Sodium Starch Glycolate, NF	Business	
Magnesium Stearate, NF		
Total	250.00 mg	

(b)4 - Confidential Business

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VINTAGE PHARMACEUTICALS, INC.
Amitriptyline HCl Tablets, USP
10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg

COMPONENTS AND COMPOSITION
STATEMENT
Amitriptyline HCl Tablets
75 mg

Ingredient	per tablet	Quantity per batch
Amitriptyline HCl, USP	75.00 mg	
Microcrystalline Cellulose, NF PH101		
Lactose Monohydrate, NF DC		
Colloidal Silicon Dioxide, NF		
Sodium Starch Glycolate, NF		
Magnesium Stearate, NF		
Total	375.00 mg	

(b)4 - Confidentia Business

(b)4 - Confidential

(b)4 - Confidential Business

10/28/96
Approved - Manufacturing Date

10/28/96
Approved - Regulatory Affairs Date

VINTAGE PHARMACEUTICALS, INC.
Amitriptyline HCl Tablets, USP
10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg

COMPONENTS AND COMPOSITION
STATEMENT
Amitriptyline HCl Tablets
100 mg

Ingredient	per tablet	Quantity per batch
Amitriptyline HCl, USP	100.00 mg	
Microcrystalline Cellulose, NF PH101	(b)4 - Confidential Business	
Lactose Monohydrate, NF DC		
Colloidal Silicon Dioxide, NF		
Sodium Starch Glycolate, NF		
Magnesium Stearate, NF		
Total	500.00 mg	(b)4 - Confidential Business

(b)4 - Confidential Business

Approved - Manufacturing 10/28/96 Date

Approved - Regulatory Affairs 10/28/96 Date

VINTAGE PHARMACEUTICALS, INC.
Amitriptyline HCl Tablets, USP
10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg

COMPONENTS AND COMPOSITION
STATEMENT
Amitriptyline HCl Tablets
150 mg

Ingredient	per tablet	Quantity per batch
Amitriptyline HCl, USP	150.00 mg	
Microcrystalline Cellulose, NF PH101		
Lactose Monohydrate, NF DC	(b)4 - Confidentia	
Colloidal Silicon Dioxide, NF	Business	
Sodium Starch Glycolate, NF		
Magnesium Stearate, NF		
Total	750.00 mg	(b)4 - Confidential Business

(b)4 - Confidential Business

Approved - Manufacturing Date 10/25/96

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